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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/487,023	01/19/2000	Parkash S. Gill	21327-701 CIP	2622

7590

02/06/2003

McCutchen Doyle Brown & Enersen LLP
Three Embarcadero Center
San Francisco, CA 94111

EXAMINER

MCGARRY, SEAN

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 02/06/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Applicati n No.

09/487,023

Applicant(s)

GILL ET AL.

Examiner

Sean R McGarry

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

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DETAILED ACTION

Claims 1, 9, 11, 13, 14, and 15 remain rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,801,156]. This rejection is maintained for the same reasons set forth in the official Action mailed 5/17/02.

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1, 9, 11, 13, 14, and 15 remain rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,710,136]. This rejection is maintained for the same reasons set forth in the official Action mailed 5/17/02.

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1, 9, 11, 13, 14, and 15 remain rejected under 35 U.S.C. 102(e) as being anticipated by Uchida et al [US 6,150, 092]. This rejection is maintained for the same reasons set forth in the official Action mailed 5/17/02.

Uchida et al disclose many antisense oligonucleotides that are targeted to the same target region those antisense disclosed in the instant specification and embraced in the instant claims and it is assumed that the antisense of Uchida et al inherently posses the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example. See Tables 1 and 2, for example.

Claims 1, 9, 11, 13, 14, and 15 remain rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,814,620]. This rejection is maintained for the same reasons set forth in the official Action mailed 5/17/02.

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1-3, 7-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Uchida et al (above) and Robinson et al [5,814,620; 5,710,136; and, 5,801,156]. This rejection is maintained for the same reasons set forth in the official Action mailed 5/17/02.

The claimed invention is antisense oligonucleotides for the inhibition of VEGF where there are several specific antisense sequences recited in the claims.

Robinson et al is relied upon as above and is relied upon to demonstrate that antisense oligonucleotides have been known for use in various methods of treatment prior to applicants invention and that it was known to use liposome formulations for pharmaceutical preparations of antisense oligonucleotides (see column 9, for example). It has been taught by Robinson et al that synthetic oligonucleotides of their invention [VEGF antisense] may be used in pharmaceutical preparation when combined with appropriate carrier. It is further taught that such compositions can include other factors and/or agents which enhance inhibition of VEGF expression or which will reduce neovascularization (see columns 8 and 9, for example).

Uchida et al have taught methods of inhibiting VEGF with antisense oligonucleotide. The antisense oligonucleotides claimed by Uchida et al are targeted, for example, to the specific region of VEGF nucleic acid SEQ ID NO: 7. All of the specifically recited antisense oligonucleotides of instant claim 2, for example, are all targeted to SEQ ID NO: 7 or Uchida et al, and further all the recited antisense

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oligonucleotides of instant claim 2 either overlap, embrace, or are embraced by the specifically claimed antisense of Uchida et al claim 7, for example (SEQ ID NOS: 51, 54, 53, 50, 49, 138, and 141 of Uchida et al, for example).

One in the art would clearly have had motivation to make the instantly claimed antisense molecules since it is absolutely clear that the region targeted has been clearly shown by the prior art to be a desired target for antisense inhibition of VEGF. Furthermore the specific antisense claimed are not only targeted to the taught target sequence but overlap, embrace or are embraced by the specific VEGF antisense taught by Uchida et al. One in the art would clearly look to these specific regions to make antisense oligonucleotides to inhibit VEGF since these specific region and antisense have been clearly taught in the art to be effective antisense oligonucleotides and target sequences. One would expect that the inhibition conditions recited in the claims would be met since these values were observed upon making antisense targeted to the specific region clearly taught in the prior art.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Claims 4-6 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Uchida et al., Robinson et al [US 5,814,620], Barleon et al [Blood Vol. 87, No. 8:3336-3343, 4/15/96] and Chan et al [The American journal of Surgical Pathology Vol. 22(7):816-826, 1998].

Uchida et al is relied upon as above and further for the following: It has been taught at column 1, for example, that "...inhibition of the vascular endothelial growth factor leads to inhibition of growth of solid tumor cells, and this should be applicable in the development of anticancer agents. [I]n fact there is a report on a method to use an anti-VEGF antibody"

Robinson et al is relied upon as above and for the following: It has been taught by Robinson et al that synthetic oligonucleotides of their invention [VEGF antisense] may be used in pharmaceutical preparation when combined with appropriate carrier. It is further taught that such compositions can include other factors and/or agents which enhance inhibition of VEGF expression or which will reduce neovascularization (see columns 8 and 9, for example).

Barleon et al taught inhibition of VEGF via specific antiserum and the role of flt-1 with VEGF biopathway.

Chan et al have taught the Association of VEGF and its receptors and their roles in various diseases.

It would have been obvious to use antibodies in conjunction with antisense targeted to VEGF since the prior art has taught antisense to inhibit VEGF, antibodies to inhibit VEGF and since the art has taught that VEGF receptors are associated with the same disease states as VEGF. The art has taught that one in the art can combine other VEGF inhibitors in combination with VEGF antisense. Since the art has shown inhibition of VEGF by antisense and via antibodies one in the art would have a reasonable expectation of the successful use of a combination of such a combination.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Applicant's arguments filed 11/25/02 have been fully considered but they are not persuasive.

Applicant offers the following arguments for all of the rejections of record. Applicant argues that none of the cited references present evidence showing inhibition of proliferation of any type of cells in culture and that the inherent property applicant asserts is the difference in the prior art and that claimed does not necessarily flow from the teachings of the prior art. First, it is noted that the instant claims do not require any specific conditions for the determination of an IC_{50} in cultured Kaposi's Sarcoma cells. Second, for example, The antisense oligonucleotides of Uchida et al are targeted, for example, to the specific region of VEGF nucleic acid SEQ ID NO: 7. All of the specifically recited antisense oligonucleotides of instant claim 2, for example, are all targeted to SEQ ID NO: 7 or Uchida et al, and further all the recited antisense oligonucleotides of instant claim 2 either overlap, embrace, or are embraced by the specifically claimed antisense of Uchida et al claim 7, for example (SEQ ID NOS: 51, 54, 53, 50, 49, 138, and 141 of Uchida et al, for example). The prior art therefore teaches the structural limitations of the claimed invention and further demonstrates that many of those instantly claimed overlap, embrace or are embraced by those antisense taught in the art where all of these antisense are targeted to the same region defined by

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SEQ ID NO:7 of Uchida et al. Applicants observation of a particular IC₅₀ is not seen as evidence of a difference between the prior art antisense and that instantly claimed.

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

“[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency’ under 35 U.S.C. 102, on prima facie obviousness’ under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted].” The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

MPEP 2112.01:

PRODUCT AND APPARATUS CLAIMS — WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TO THAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS ARE PRESUMED TO BE INHERENT

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

COMPOSITION CLAIMS - IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES

“Products of identical chemical composition can not have mutually exclusive properties.” A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)

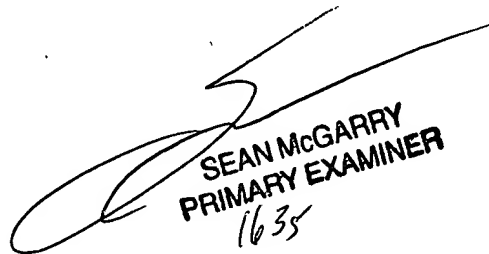
Based on the disclosure and teachings of the prior art and the cites above it is clear that the burden was properly shifted to applicant after the mailing of the Official Action mailed 5/17/02. It is applicants burden to provide evidence of an unobvious difference between the prior art and that instantly claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SRM
February 5, 2003


SEAN McGARRY
PRIMARY EXAMINER
1635